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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION See Form PCT/IPEA/416	
100647-1 WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE 2003/000617	15.04.2003	19.04.2002
International Patent Classification (IPC) or national classification and IPC		
C07D 473/20, C07D 473/22, A61K 31/52, A61K 31/522, A61P 25/28, A61P 35/00		
Applicant		
AstraZeneca AB et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
31.10.2003	20.07.2004
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Per Renström/BS Telephone No. +46 8 782 25 00

INTERNATIONAL PRELI[redacted]RY REPORT ON PATENTABILITY

Int[redacted]onal application No.
PCT/SE 2003/000617

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))
☐ publication of the international application (under Rule 12.4)
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ the claims:

pages _____ as originally filed/furnished
pages* _____ as amended (together with any statement) under Article 19
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIM[redacted]RY REPORT ON PATENTABILITY

Int[redacted]nal application No.
PCT/SE 2003/000617

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 7 partly

because:

☒ the said international application, or the said claims Nos. 10
relate to the following subject matter which does not require an international preliminary examination *(specify)*:

See PCT Rule 67.1.(iv).: Methods for treatment of the human or animal body therapy.

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 7 partly
are so unclear that no meaningful opinion could be formed *(specify)*:

The initial phase of the search revealed a very large number of documents potentially relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of claim 7 may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim is impossible. Consequently, the search regarding the first medical indication has been restricted to a very small sample of the large number of documents found.

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in the Annex *C-bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE 2003/000617

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	6,8-9,11-12	YES
	Claims	1-5,7	NO
Inventive step (IS)	Claims	-	YES
	Claims	1-9,11-12	NO
Industrial applicability (IA)	Claims	1-9,11-12	YES
	Claims	-	NO

2. Citations and explanations (Rule 70.7)

Documents from the International Search Report:

D1: WO 9618400 A1
D2: EP 01016407 A1
D3: EP 0430300 A2
D4: US 5756511 A
D5: US 5173491 A
D6: WO 0185146 A1
D7: WO 9936073 A1

The present invention relates to thioxanthine derivatives with use in the treatment of neuroinflammatory disorders and other diseases or conditions in which inhibition of myeloperoxidase (MPO) is beneficial.

D1 (see especially page 5, lines 23-25; page 5, line 29 - page 6, line 21 and page 7, lines 3-26), representing the closest prior art, describes thioxanthines for use in the treatment of asthma, inflammation and dementia. Several of the preferred compounds in D1 satisfy formulas (1a) and (1b) in claim 1, as well as the requirements of claims 2-5 and 7 in the present application.

Since asthma and dementia are diseases in which MPO inhibition may be beneficial, and since dementia and inflammation may be neuroinflammatory disorders, the invention according to claims 1-5 actually lacks novelty with regard to D1. The invention according to claim 7, directed to the first medical indication for the compounds, also lacks novelty with regard to D1.

.../...

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The expression "diseases or conditions in which inhibition of the enzyme MPO is beneficial" in claim 1 may relate to a large number of different disorders which cannot be clearly defined by this expression. The claim does not meet the requirements of Article 6 PCT that claims shall be clear and concise.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box No. V

The invention according to claims 6, 8-9 and 11-12 relates to compounds that have one of the following differences compared to the preferred compounds in D1: (1) R^1, R^2, R^3 or R^4 is H instead of alkyl, (2) X and Y, representing S and O, are shifted, or (3) R^1, R^2 or R^4 represent other alkyls.

The invention according to claims 6, 8-9 and 11-12 can with these substitutions be thought of as a set of solutions to the general problem of providing alternative medicines against certain disorders, for example dementia and asthma.

However, since such substitutions are common practise in drug development and therefore generally are considered obvious to the person skilled in the art, the invention according to claims 6, 8-9 and 11-12 is, in the absence of any shown unexpected and beneficial effects of the new derivatives, considered to lack an inventive step in view of D1.

Documents D2-D7 only represent the general state of the art and are of no particular relevance.

In summary, the invention according to claims 1-5 and 7 lacks novelty and the invention according to claims 1-9 and 11-12 is considered to lack an inventive step.